Surveillance Strategies in Kidney Cancer: When is Enough?

---

Role of Survivorship Clinic in Long-Term Follow-Up of Kidney Cancer

Brandon Manley, MD
Assistant Member, Genitourinary Oncology
WHO classification of tumours of the kidney

<table>
<thead>
<tr>
<th>Renal cell tumours</th>
<th>Mesenchymal tumours occurring mainly in adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clear cell renal cell carcinoma</td>
<td>Leiomyosarcoma</td>
</tr>
<tr>
<td>Multilocular cystic renal neoplasm of low malignant potential</td>
<td>Angiosarcoma</td>
</tr>
<tr>
<td>Papillary renal cell carcinoma</td>
<td>Rhabdomyosarcoma</td>
</tr>
<tr>
<td>Hereditary leiomyomatosis and renal cell carcinoma–associated renal cell carcinoma</td>
<td>Osteosarcoma</td>
</tr>
<tr>
<td>Chromophobe renal cell carcinoma</td>
<td>Synovial sarcoma</td>
</tr>
<tr>
<td>Collecting duct carcinoma</td>
<td>Ewing sarcoma</td>
</tr>
<tr>
<td>Renal medullary carcinoma</td>
<td>Angiomyxipoma</td>
</tr>
<tr>
<td>MIT family translocation renal cell carcinomas</td>
<td>Epithelioid angiomyxipoma</td>
</tr>
<tr>
<td>Succinate dehydrogenase–deficient renal carcinoma</td>
<td>Leiomyoma</td>
</tr>
<tr>
<td>Mucinous tubular and spindle cell carcinoma</td>
<td>Haemangiomata</td>
</tr>
<tr>
<td>Tubulocystic renal cell carcinoma</td>
<td>Lymphangiomata</td>
</tr>
<tr>
<td>Acquired cystic disease–associated renal cell carcinoma</td>
<td>Haemangioblastoma</td>
</tr>
<tr>
<td>Clear cell papillary renal cell carcinoma</td>
<td>Juxtaglomerular cell tumour</td>
</tr>
<tr>
<td>Renal cell carcinoma, unclassified</td>
<td>Renomedullary interstitial cell tumour</td>
</tr>
<tr>
<td>Papillary adenoma</td>
<td>Schwannoma</td>
</tr>
<tr>
<td>Oncocytoma</td>
<td>Solitary fibrous tumour</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Metanephric tumours</td>
<td>Mixed epithelial and stromal tumour family</td>
</tr>
<tr>
<td>Metanephric adenoma</td>
<td>Cystic nephroma</td>
</tr>
<tr>
<td>Metanephric adenofibroma</td>
<td>Mixed epithelial and stromal tumour</td>
</tr>
<tr>
<td>Metanephric stromal tumour</td>
<td>8959/0</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Nephroblastic and cystic tumours occurring mainly in children</td>
<td>Neuroneuroendocrine tumours</td>
</tr>
<tr>
<td>Nephrogenic rests</td>
<td>Well-differentiated neuroendocrine tumour</td>
</tr>
<tr>
<td>Nephroblastoma</td>
<td>Large cell neuroendocrine carcinoma</td>
</tr>
<tr>
<td>Cystic partially differentiated nephroblastoma</td>
<td>Small cell neuroendocrine carcinoma</td>
</tr>
<tr>
<td>Paediatric cystic nephroma</td>
<td>Phaeochromocytoma</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Mesenchymal tumours</td>
<td>Miscellaneous tumours</td>
</tr>
<tr>
<td>Mesenchymal tumours occurring mainly in children</td>
<td>Renal haematopoietic neoplasms</td>
</tr>
<tr>
<td>Clear cell sarcoma</td>
<td>Germ cell tumours</td>
</tr>
<tr>
<td>Rhabdoid tumour</td>
<td></td>
</tr>
<tr>
<td>Congenital mesoblastic nephroma</td>
<td>Metastatic tumours</td>
</tr>
<tr>
<td>Ossifying renal tumour of infancy</td>
<td></td>
</tr>
</tbody>
</table>

The morphology codes are from the International Classification of Diseases for Oncology (ICD-O) (917A). Behaviour is coded: /3 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III neoplastic lesions; and /3 for malignant tumours. The classification is modified from the previous WHO classification (756A), taking into account changes in our understanding of these lesions.

*New code approved by the IARC/WHO Committee for ICD-O.
Learning objectives

- What is the range of growth rate of small renal masses

- What is the recommended follow up imaging schedule for low and moderate/high risk renal cancer patients after surgery

- What are some of the reasons a survivorship clinic may be beneficial to both patients and providers
Natural History of Renal Masses

- For small renal masses (SRMs) mean growth rate between 0-1.6cm/year.
  - No growth ≠ No cancer
  - “Trigger” for intervention ~0.5cm/year
  - No known associations with growth

- Risk of developing metastatic disease for SRM is small but not zero.
  - About 1-2% risk depending on cohort

- Complex Cystic Masses (Bosniak IIF-IV) can safely be followed, while growth rates are lacking, surgical series show favorable histology (82% of 65 masses with pT1-T2; FG 1-2 or indolent tumors)

Smaldone MC; *Cancer* 2012
Pierorazio PM; *Eur Uro* 2015
Chandrasekar T; *J Urology* 2017
Active Surveillance for SRMs

The Delayed Intervention and Surveillance for Small Renal Masses (DISSRM) prospective registry was established in 2009.

- prospectively evaluate outcomes for patients with SRMs choosing primary intervention (PI) or AS
- Had at least 3 imaging studies

Pierozzo PM; J Urology 2017
## Selecting Patients for AS

<table>
<thead>
<tr>
<th>Favor Active Surveillance/Expectant Management</th>
<th>Patient-related factors</th>
<th>Tumor factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elderly</td>
<td>Tumor size &lt;3cm</td>
<td></td>
</tr>
<tr>
<td>Life expectancy &lt;5 years</td>
<td>Tumor growth &lt;5mm per year</td>
<td></td>
</tr>
<tr>
<td>High comorbidities</td>
<td>Non-infiltrative on imaging</td>
<td></td>
</tr>
<tr>
<td>Excessive perioperative risk</td>
<td>Low complexity</td>
<td></td>
</tr>
<tr>
<td>Poor functional status</td>
<td>Favorable histology (if RMB performed)</td>
<td></td>
</tr>
<tr>
<td>Marginal renal function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient preference to avoid treatment risks</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Favor Intervention</th>
<th>Patient-related factors</th>
<th>Tumor factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young</td>
<td>Tumor size &gt;3cm</td>
<td></td>
</tr>
<tr>
<td>Life expectancy &gt;5 years</td>
<td>Tumor growth &gt;5mm per year</td>
<td></td>
</tr>
<tr>
<td>Low comorbidity</td>
<td>Infiltrative on imaging</td>
<td></td>
</tr>
<tr>
<td>Acceptable perioperative risk</td>
<td>High complexity</td>
<td></td>
</tr>
<tr>
<td>Good functional status</td>
<td>Unfavorable histology (if RMB performed)</td>
<td></td>
</tr>
<tr>
<td>Anticipate adequate renal function following intervention</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient preference for treatment</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Stratifying risk and benefits in follow after surgery

http://labs.fccc.edu/nomograms/
Risk and Scans

Low Risk (pT1a-b)

- CXR yearly x 3 (AUA, NCCN)
- Lung most common and most favorable site of relapse
- CXR>CT Chest due lower false positive (AUA)
- Yearly Abdominal Imaging (CT, MRI or US) x 3
- After 3 years recurrence <5%

<table>
<thead>
<tr>
<th>Stop at 3 years</th>
<th>Keep going....</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (young pts needs genetics)</td>
<td>Unfavorable pathology (sarcomatoid)</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>Long life expectancy</td>
</tr>
<tr>
<td>Favorable pathology</td>
<td>Patient anxiety</td>
</tr>
<tr>
<td>Duplicate Imaging</td>
<td>Family history (genetics negative)</td>
</tr>
</tbody>
</table>
Risk and Scans

Moderate to High Risk (>pT2-T4, +N, +margin)

• Chest CT or CXR Q6 months x 5 years (AUA, NCCN)
• CT/MRI/US Abdominal, Pelvis Q6 months x 5 years (AUA, NCCN)
• Risk of recurrence 30-70%!

<table>
<thead>
<tr>
<th>CT</th>
<th>MRI</th>
<th>US</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hx Kidney stones</td>
<td>Small Aggressive Tumors</td>
<td>Age</td>
</tr>
<tr>
<td>Cost</td>
<td>Positive/Close Margin</td>
<td>Duration of follow up</td>
</tr>
<tr>
<td>Patient preference</td>
<td>CKD</td>
<td>Favorable pathology</td>
</tr>
<tr>
<td></td>
<td>Complex Cyst</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hereditary component</td>
<td></td>
</tr>
</tbody>
</table>

CXR
- Favorable pathology
- pT2
- Young Age

Chest CT
- Unfavorable pathology
- pT3/T4
- N1
- Smoker/Hx

Campbell S; Renal Mass...AUA Guidelines 2017
Active surveillance in metastatic renal-cell carcinoma: a prospective, phase 2 trial

Brian I Rini, Tanya B Dorff, Paul Elson, Cristina Suarez Rodriguez, Dale Shepard, Laura Wood, Jordi Humbert, Linda Pyle, Yu-Ning Wong, James H Finke, Patricia A Rayman, James M G Larkin, Jorge A Garcia, Elizabeth R Plimack

• Prospective phase 2 trial, enrolled patients with treatment-naive, asymptomatic, metastatic renal-cell carcinoma from five hospitals in the USA, Spain, and the UK.
• Patients were radiographically assessed at baseline, every 3 months for year 1, every 4 months for year 2, then every 6 months thereafter.
• Between Aug 21, 2008, and June 7, 2013
  • 48 patients included in analysis
  • median time on surveillance from until initiation of systemic therapy 14.9 months (95% CI 10.6–25.0).
• Factors associated with shorter surveillance
  • More IDMC risk factors
  • More metastatic sites of disease
Employing survivorship clinic to standardize follow up

• Facilitates a **team approach** to the long term care of patients

• Can address **provider-level challenges** (time, patient volume) surrounding communication and coordination of care

• Assist in keeping asymptomatic patients (especially long after acute treatment) aware of the risk of their disease and potential **toxicity** from treatment (CKD, HTN etc.)

• Models of care should be patient-centered with consideration of **access and navigation** with in and outside the treating center for each individual survivor.
Considerations to starting survivorship clinic

• High demand for acute treatment and management of patients with active disease
• Ability to stratify patients risk of recurrence (low vs. high)
• Complexities and level of toxicities associated with cancer treatment (medical and surgical)
• Institutional resources (time, space, money) and personnel (APPs, PA, nurses, physicians)
• Burden for start up and “learning curve” can seem high but long term benefits to patients and providers is evident
Question

Which tumor or patient factor is considered to favor active surveillance for a renal mass?

A. Young age
B. Poor renal function*
C. Tumor >3cm
D. Infiltrating tumor appearance on imaging

*=correct answer